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# **Socioeconomic effects on breast cancer survival: the role of stage and morphology**

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**Biostatistics Unit**

**Institute of Public Health**

**Cambridge – UK**

**Dissertation submitted to the Open University for the Degree of  
Master of Philosophy in Epidemiology**

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# SUMMARY

**Background:** Breast cancer patients of lower socioeconomic status tend to have poorer survival. This does not seem to be attributed solely to stage at presentation, but there is uncertainty as to the proportion of the survival deficit that is due to stage, and whether this is affected by the method of determining socioeconomic status. In this study, we estimate the extent to which the differences in survival by socioeconomic status, measured both by occupational and area-based methods, can be explained by differences between socioeconomic groups in stage and morphological type of tumour.

**Method and materials:** We studied survival in 10,865 cases from the East Anglian Cancer Registry diagnosed between 1982 and 1993.

**Results:** In univariate analyses, lower social class was associated with relative hazards of 1.25 (95% CI, 1.14-1.38) for death from all causes and 1.32 (95% CI, 1.12-1.55) for death from breast cancer as underlying cause. Women resident in the most deprived area had relative hazards of 1.29 (95% CI, 1.16-1.45) for death from all causes and 1.21 (95% CI, 0.95-1.54) for death from breast cancer as underlying cause. Stage at diagnosis accounted for 28% of the effect of social class on survival to death from breast cancer. For survival to death from any cause, stage accounted for 63% of the effect of social class and 31% of the effect of deprivation category.

**Discussion:** The major finding is that we could not wholly or even largely account for socioeconomic effects on breast cancer survival by pathological factors including stage and



morphology. It is concluded that stage at presentation explains some of the socioeconomic differences in breast cancer survival. Future research on histological grade and socioeconomic status is indicated. It would be useful to confirm these findings in additional studies that include other individual socioeconomic indices in addition to area-based and occupational measures.

# CHAPTER 1

## 1. Introduction, Objectives and Methods

### 1-1. Background

Breast cancer has become a major health problem over the last 50 years, affecting as many as one in eight women during their lifetime (Ries, 1999; Sondick, 1994). This disease is a significant health problem in the industrialised western world, where it is the most common form of cancer among women in North America and almost all of Europe (Forbes, 1997).

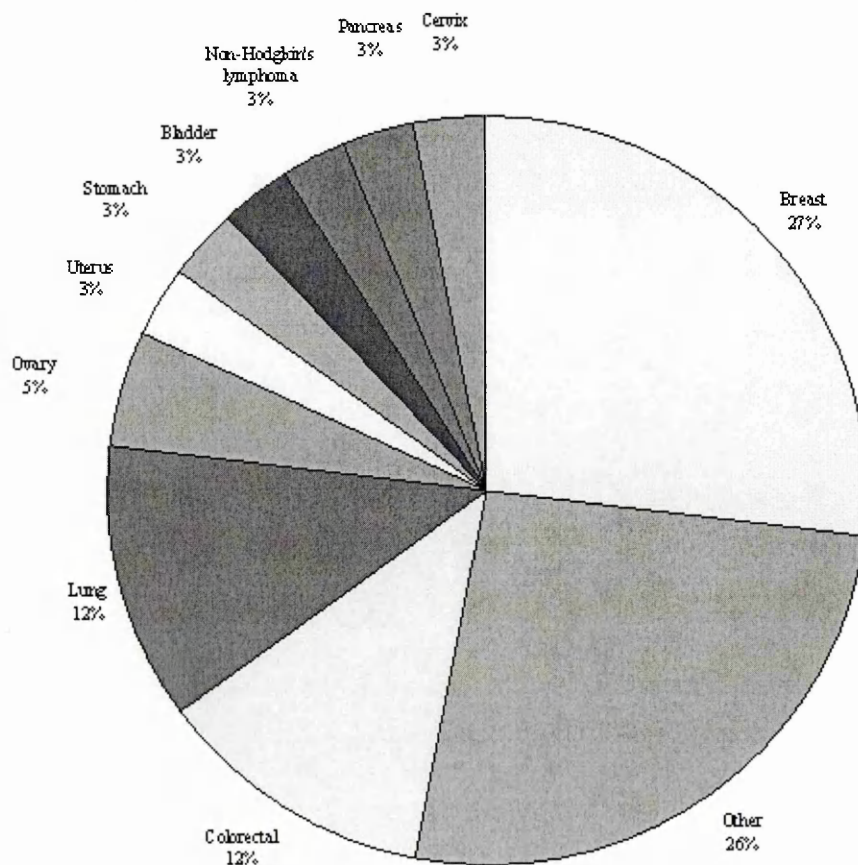
Breast cancer has been the subject of extensive epidemiologic studies, which have provided insight into the magnitude of this problem and identified factors that place women at increased risk for the development of this malignancy. There is substantial variation in breast cancer rates in women among different countries. Over one million new cases are diagnosed in women worldwide every year, causing over 400,000 deaths (Forbes, 1997).

Breast cancer is the most common cancer in women in England and Wales, responsible for about 30 % of all female malignancies and about 20% of female cancer deaths (Swerdlow et al, 2001). There were 27,768 new registrations of breast cancer in 1989 (Cancer- statistics, 1989).

13,663 deaths were attributed to breast cancer in 1992 (OPCS, 1992). The age standardized incidence rate of this disease was 68.2 per 100,000 for England and Wales.

The number of new breast cancer cases was increased to 33,829 in year 2000, which was about 30 % of all cancers in women (Figure 1-1)

**Figure 1-1.** Comparison of breast cancer to other common cancers in women in UK (National Statistics 2000).



Survival from breast cancer has improved gradually over time due to earlier detection of tumour, use of effective adjuvant therapy and, more recently, the introduction of Breast Screening Programme (Coleman et al, 1999; Berrino, 1995).

## **1-2. Socioeconomic status and cancer mortality**

The effect of socioeconomic status (SES) differences in mortality has been reported for a variety of causes of death including cancer (Carola, 1994). Cancer mortality is generally higher in people of low socioeconomic status compared with those of higher socioeconomic status (Kogevinas et al, 1991). This mortality penalty may be due to differences in cancer incidence or cancer survival. Socioeconomic status (SES) can be considered as a “cross-cutting risk factor”, which means that it may be simultaneously related to incidence by the risk for developing cancer, as well as to survival from the disease (Baquet et al 2000).

Understanding socioeconomic differences in cancer incidence and cancer survival is not only of academic interest; such information is required to design health policy measures.

Differences in cancer incidence demand intervention in the area of primary prevention, whereas socioeconomic differences in cancer survival demand policy measures in the area of secondary prevention or treatment (Carola 1994).

Socioeconomic differences in cancer survival, if not an artefact, may be related to differences in timing of diagnosis, in treatments applied, in biological characteristics of the neoplasm or in

host factors, including comorbidity (Vågerö & Persson, 1987). Several studies from different countries, based on mortality and morbidity data have shown that survival from cancer is associated with socioeconomic position or social class (Vågerö & Persson, 1987; Carnon et al, 1994; McLoad et al, 2000; Schrijvers et al, 1995; Karjalainen et al, 1990).

In a survival analysis, Garvican et al (1998) found breast tumours in deprived women were more likely to have positive node status, suggesting that the relationship between deprivation and prognosis is due to more advanced stage at presentation in more deprived patients. Vågerö & Persson (1987) studied the effect of socioeconomic status according to patient's occupation by using the Swedish cancer registry data, finding a clear difference in relative survival for breast cancer. The pattern showed better survival for those with higher socioeconomic status. Baquet et al (2000) found that people with lower income had a death rate double that observed in people with income above the poverty level. These results suggested that inequalities in mortality and survival may be related to health care access and insurance status, income, educational status, health care seeking behaviour, diagnosis and treatment quality.

### **1-3. Breast cancer survival and deprivation based on area of residence**

Research on the relationship between mortality and deprivation, based on area of residence has showed a strong association with several health outcomes, including cancer (Taylor et al, 1997).

A number of studies have analysed differences in the incidence and survival for various cancers (Kogevinas et al, 1990; Schrijvers et al, 1994). This would affect patients beyond their individual characteristics, stressing the importance of indicators and targets to monitor improvements around geographical areas. This approach considers patients not only as individuals, but also as individuals related to their environment, whose inequalities might have health repercussions (Carstairs, 1989). Deprivation indexes may potentially be used as a surrogate for health inequalities, as well as for those social conditions likely to affect survival.

Using the area of residence as a measure of deprivation has been justified on theoretical grounds as it has been correlated with a range of health measures, including incidence and mortality (Scottish Office, 1998; Townsend, 1986). The indices of deprivation according to area of residence can be designed using a range of small area statistics accessible from routinely collected census data (Jarman, 1983). The analysis of health data based on area of residence is feasible due to the use of postcodes, which accompany most health related data (Harris et al, 1998). The ease with which the data are accessed reduces substantially the costs of the analysis if compared to those studies where further data collection is required.

#### **1-4. Breast cancer survival and social class based on occupation**

Studies of social class and health show poorer health and shorter life expectancy in general for the deprived people. The degree of the difference, however, varies with the measures

used and the social group being studied. Furthermore, the social class indicator used influences the results. Social class is defined in the UK by subject's occupation or occupation of the subject's spouse.

Differences in mortality related to social class have been reported for several diseases, including tumours. Stage at diagnosis has been shown to be an important factor contributing to social class differences in cancer survival. Nevertheless, the importance of stage seems to vary by type of tumour and by country. Also, definitions are hard to standardize. For instance, the meaning of the terms "class" or "social class" are complex. So far, to add accuracy, "occupational class" term has been used in European public health surveillance and research. The British Registrar General's social class schema is the longest employed of these measures, developed by the Registrar General THC Stevenson in 1913. This approach conceptualized occupations as a measure of what was termed "standing within the community" or "culture". This representation has proven to be predictive of inequalities in morbidity and mortality. It comprises five categories, as follows:

Social class I (professional), II (intermediate), IIINM (skilled non-manual), IIIM (skilled manual), IV (partly skilled), and V (unskilled). In this sense, distinctions between different social classes levels are based on a graded hierarchy of occupations ranked according to skill.

One limitation of using socioeconomic indicators based on occupation in the UK, mainly for breast cancer, is that women workers are concentrated into fewer and less well paid occupations comparing to men, in each level of the Registrar General's social class. An additional liability of occupation-based measures is that they cannot readily be used for social groups outside of the recognized paid labour force. Among those groups, we can include retired adults who are unemployed and homemakers (chiefly women) who do not work

outside of home. In the past, husband's occupation has been used to define a women's social class.

## **1-5. Review of literature**

The first study to find an association between socioeconomic status and breast cancer survival was conducted by Cohart in 1955. Later on, a large difference was found among ethnic groups in the US (Young 1981). Since then, the relationship between breast cancer and socioeconomic deprivation has proved to be complex and studies have so far have provided equivocal and inconclusive results. This is because although most studies found poorer survival in lower SES groups, the magnitude of the difference and the extent to which of is attributed to stage or other factors vary between studies. Thus, the relation between deprivation and breast cancer survival is not fully understood.

Affluent women have a higher incidence of breast cancer than those socially deprived.

Regarding prognosis, several studies have shown that deprived women have poorer survival from breast cancer (Carnon et al, 1994; Macleod et al, 2000; Schrijvers et al 1995, Karjalainen et al 1990).

It is possible that women of lower socioeconomic present with late stage disease because of a combination of decreased access to medical care and decreased awareness of the importance of early cancer detection. The role of ethnic differences as a possible index for socioeconomic status in survival from breast cancer has also been reported in the US (Young et al, 1981; Richardson et al, 1992; Eley et al, 1994; Hsu et al 1997; Hunter 2000). Freeman & Wasfie



(1989), in a retrospective study on disparity of breast cancer survival concluded that inequality in survival for poor black women compared with black women nationally, and with white women, was due to late stage of disease at diagnosis. They found that about 49% of poor black women presented their cancer with stage III and Stage IV. Therefore, they believed that late diagnosis was the single most important factor responsible for inequality of survival in their study. Also for example, Bibb et al (2000) studied the survival of patients with breast cancer in the US, comparing African American against white women. The results revealed that the late stage of breast cancer was more likely to be diagnosed in African American women with low socioeconomic status.

Thus, women from deprived areas or groups are less likely to get breast cancer, but experience poorer survival than their more affluent counterparts. The combined effect on mortality is usually to the detriment of the lower SES groups. The cause for this differential mortality experience remains uncertain. It is probably multifactorial. A number of reasons have been proposed, including differences in tumour stage, tumour biology, treatments or host response (Garvican & Littlejohns 1998).

Schrijvers et al (1995) have shown differences of 35% in survival rates in favour of affluent women over deprived women, for all ages. Carnon et al (1994) also found significantly worse survival from breast cancer in socio-economically deprived groups after adjustment for stage of disease. Dayal et al (1982) looked at the effect of race and socioeconomic status, and found that both produced different survival patterns. Basset et al (1986) found that social class was a significant factor in determining survival after a diagnosis of breast cancer, with a relative risk of 1.52 (95% CI, 1.28-1.88) for deprived as opposed to affluent women. Vågerö & Persson (1987) also found differences in survival by social class in a study of Swedish cancer patients.

Socioeconomic differences in breast cancer survival have been reported in studies from the US, Finland, Sweden, Australia, Scotland and England and Wales. Large socioeconomic differences in breast cancer survival have been observed in England and Wales (Coleman et al 1999). Exceptionally, one study showed that breast cancer patients of low socioeconomic status had a higher (although only slightly) chance of survival from their disease than breast cancer patients of higher social classes (Kogevinas 1991). However, they defined high and low socioeconomic groups by whether the patients were homeowners or council tenants. They excluded those who did not fit either of these categories from their study. Another problem with using such a crude measure of socio-economic status is that it is likely to misclassify very large numbers of patients, as being deprived and council tenant status are not synonymous. For instance, in some areas of England there can be high levels of home ownership coupled with high levels of overcrowding, which on most definitions of deprivation is somewhere near the top of the list of indicators.

Many studies that have examined the effect of socio-economic status on breast cancer survival have included the age of patients as a possible confounding variable to be adjusted for in the analysis. For example, Dayal et al (1982) found that in 5-year survival after breast cancer, patients aged 40-59 had higher survival, followed by those aged over 60. Patients under 40 had the worst prognosis. However, looking at the longer-term survival (10 years), they found that there was an inverse relationship between age at diagnosis and survival probabilities, although the differences were not statistically significant. Ansell et al (1993) also found a non-significant relative risk of 1.06 due to adjusting for age as a confounder of socioeconomic status.

The study by Carnon et al (1994) also found differences in survival by age-group, with those aged less than 44 having the highest survival times, and those aged between 55 and 76 having the lowest survival. Schrijvers et al (1995) found a steeper gradient between socio-economic groups in the 65-99 age group than in the under 64 group, although this difference was accounted for when adjusting for stage of the cancer at diagnosis, the morphology of the cancer, and the type of treatment undertaken.

Table 1 shows the relative risk for fatality reported in different studies, according to socioeconomic differences.

**Table 1-1: Socio-economic differences in survival from breast cancer (Garvican & Littlejohns 1998).**

Reference, country	SES by various measures	Relative risk (95% CI)		Comments
Auvinen, 1995 Finland	I	0.75	(0.65-0.86)	Risk ratio adjusted for age and year of diagnosis. Five year cumulative survival: class I, 77%, class II, 75%, class III, 73% Class IV, 72%.
	II	0.85	(0.76-0.94)	
	III	0.93	(0.85-1.03)	
	IV	1.0		
Bassett & Krieger, 1986, US	High	1.0		Relative risk adjusted for race, age, stage and histology.
	Low	1.52	(1.28-1.88)	
Burnett et al, 1993 Australia	High	1.0		Cox regression analysis was performed.
	Low	1.35	(1.00-1.70)	
Karjalainen & Pukkala, 1990 Finland	I	0.78	(0.68-0.90)	Risk ratio adjusted for age. Follow-up, period of diagnosis stage, and the interaction of stage and follow-up period.
	II	0.85	(0.77-0.93)	
	III	0.92	(0.88-0.97)	
	IV	1.0		
LeMarchand et al. 1984; US	High	1.0		Relative risk (95% CI), adjusted for age, stage, race, histology and marital status.
	Medium	0.96	(0.77-1.20)	
	Low	1.23	(0.97-1.57)	
Schrijvers et al, 1995a, England	Affluent	1.0		Cox regression adjusted for follow-up period and period of diagnosis. Women aged 30-64.
	2	1.15	(1.05-1.27)	
	3	1.30	(1.18-1.44)	
	4	1.31	(1.18-1.46)	
	Deprived	1.35	(1.16-1.57)	
Schrijvers et al 1995b, The Netherlands	High	1.0		Cox regression adjusted for age and period of follow-up.
	2	1.06	(0.84-1.33)	
	3	1.04	(0.86-1.26)	
	4	1.15	(0.96-1.38)	
	Low	1.18	(0.99-1.42)	
Boffeta et al, 1993 Italy	>or=7 year	0.70	(0.40-1.10)	Relative risk adjusted for age. SES based on education.
	<7 year	1		
Kogevinas et al, 91 England and Wales	Owner occupier	0.99		Standardized case fatality ratio. Crude five-year survival: 50% for owner occupiers, and 52% for council tenants.
	Council tenant	0.97		
Waxler-Morrison et al, 1991, Canada	Employed	1.0		Cox regression adjusting for nodal status, stage, marital status.
	Not -employed	1.52		
Rosso et al, pers. Commun, Italy.	University	0.89	(0.54-1.49)	Relative risk adjusted for age, place of birth and housing.
	High	0.94	(0.70-1.27)	
	Middle	1.01	(0.99-1.51)	
	Low	1.0		
Nandacumar et al 1995; India	Illiterate	1.0		Relative risk (95% CI), adjusting for religious group, marital status and clinical extent of the disease. Five-year survival rates were 35%(illiterate) and 46% (literate)
	Literate	0.7	(0.60-0.80)	
Gordon et al., 1992 US	High	1.00		Cox regression
	Low	1.49	(1.17-1.89)	

## 1-6. Objective

This study is an analysis of survival data, to examine the effect, if any, of socioeconomic status at the time of diagnosis on survival. A univariate analysis will be performed first. Thereafter, a series of multivariate Cox regression models will be fitted, in which socioeconomic status will be adjusted for.

In particular, we were interested to see which factors caused alteration of the SES effects on survival when adjusted for in a multivariate model. Potential influences on survival in breast cancer include the stage at diagnosis, the tumour type (morphology), and histological grade. These could be confounded with SES in various ways, and each would be responsible to a greater or lesser extent for the observed poorer survival in women of low SES.

The simplest example is stage of disease at diagnosis. This is a combination of size of the tumour in the breast and the extent to which it has spread beyond the breast, in particular to the regional lymph nodes. If, for example, women of low SES were less aware of breast symptoms or less likely to receive mammography screening, they would have later stage at diagnosis, and adjustment for stage in a multivariate survival model would tend to attenuate the estimated effect of SES on survival. If this were the case, the target for public health would be education on breast symptoms and efforts to improve participation of women of lower SES in screening.

Morphological type of tumour is its innate structure as observed microscopically by the pathologist. For this study, morphology was coded as:

Group 1: *Ductal carcinoma.*

Group 2: *Medullary carcinoma*

Group 3: *Lobular carcinoma*

Group 4: *Mucinous & Tubular carcinoma*

Group 5: *Adenocarcinoma, not otherwise specified*

Group 6: *Other morphology*

Different types of tumours are associated with different survival (Tabar et al, 1996). In addition, they have different risk factors (Duffy et al, 1999). Due to differences in risk factor prevalences or to genetic effects, low SES women might be more prone to the more severe morphological types. This would be manifested in a reduction in the effect of SES after adjustment for type. Such a phenomenon would suggest that measures aimed at primary prevention and better access to treatment would be the appropriate public health targets.

Histological grade is a combination of microscopic measurements, scored 1-3 with 1 representing good prognosis, 2 intermediate and 3 poor. It has in the past been thought to be innate and unchanging within the tumour although there is now evidence that it deteriorates as the tumour grows (Tabar et al 1996). Thus if grade were responsible for the effect of SES, a combination of measures aimed at prevention, screening and treatment would be indicated as targets for public health.

## **1-7. Survival time calculation**

In the primary survival analysis we used only those tumours diagnosed in 1982-1993. This was because prior to 1982, the data on stage, morphology etc was usually not available. We used data on cases prior to 1994 because for these subjects tumour data and follow up to the end of 1998 were considered to be complete.

Survival time was calculated as the time difference, in years, between date of diagnosis and date of death or December 31, 1998, for those who did not die during the follow-up period. Date of diagnosis used to calculate survival time was that obtained from chart review. For the analysis of breast cancer only deaths, patients dying of causes other than breast cancer were censored on their date of death.

## **1-8. Measures of SES used**

In this study, the simple index of Carstairs and Morris (1989) was used. It is based on the categorisation of the 1991 census-derived deprivation score at enumeration districts level (Pollock 1997). In order to estimate the socio-economic status of the patients, a surrogate measure is used, due to the difficulties in classifying women by occupation. As an example of such difficulties, Carstairs and Morris (1989) reported that in the 1981 census, 42% of women aged 16-64 were not assigned to an occupation on their own account.

The Carstairs and Morris deprivation index uses the following four variables, defined as follows:

“Overcrowding”: The persons in private households living at a density of more than one person per room.

“Male unemployment”: The proportion of economically active males who are seeking a job.

“Low social class”: The proportion of all persons in private households with head of household in social class 4 or 5.

“No Car”: The proportion of all persons in private households with no car.

Each of these variables are summed for a small geographical area based on census enumeration districts, having first been standardised by subtracting the mean for Great Britain as a whole, and dividing by the population standard deviation. All the Carstairs scores are then ranked for the whole of Great Britain. Each census enumeration district was then assigned a deprivation category, from 1 (affluent) to 5 (deprived). The deprivation score for each woman then was found by linking the postcode of her home to the corresponding census enumeration index, as described by Schrijvers et al (1995).

## **1-9. Descriptive analysis**

Before detailed survival analysis, statistics were generated to compare the characteristics of women who were categorised in different socioeconomic levels. The relationship of each covariate to socioeconomic status was examined by tabulation, and likelihood ratio chi-squared statistics were calculated to assess whether differences in proportion between the exposure groups could be attributed to random variation.



The relationship of each covariate to the outcome of interest (survival) was examined by modelling each variable individually, adjusted and unadjusted, using Cox's proportional hazards model. Survival estimates were obtained using the Kaplan-Meier estimate.

# **CHAPTER 2**

## **2. Data available**

### **2-1. Introduction**

In this chapter, the data source and explanatory variables will be introduced, as well as the manner in which the variables were coded to ease the analysis. The rationale used to decide which variables were studied will also be explained. This thesis is intended to cover the major prognostic factors stage at presentation, grade and morphology of tumour, which might contribute to socio-economic differences in breast cancer survival.

### **2-2. East Anglian Cancer Registry (EACR)**

This study uses data from the East Anglian Cancer Registry (EACR). The EACR was established in 1989 by the union of registries in Cambridge, Norwich and Ipswich. The registry holds computerised information since 1971, on cancers diagnosed in residents of Cambridgeshire, Norfolk and Suffolk, which have a combined population of approximately two million (population estimates unit, 1991:OPCS).

Information is sought by the EACR from a variety of sources including pathology laboratories, death certificates, hospital information systems, general practitioners, medical records, post mortem reports, and radiotherapy units. The registry is located in Cambridge with satellite bureaux in Norwich and Ipswich.

The EACR is the only UK registry with a system of “active follow up”. Vital status is sought on patients at three years and at subsequent five-year intervals until death. This has the advantage of providing several opportunities to collect data that may be unavailable at initial registration. The current data-set includes all items on the National Minimum Data-set, vital status at follow up, and causes of death.

### 2-3. Breast cancer by year

For this study, data were available on cases diagnosed in four major hospitals in the East Anglian region. These hospitals were Addenbrooke's, Norfolk & Norwich, Ipswich and West Suffolk. Between 1982 and 1993 a total of 10865 breast cancer cases were diagnosed in these hospitals. The number of cases in different years between 1982 and 1993 is shown in table 2-1. This table shows that the number of breast cancers increased gradually over the years of study.

**Table 2-1.** Distribution of breast cancer by year of diagnosis in four major hospitals, in the East Anglian Region, 1982-1993.

Year	No of cases	Percent	Cumulative (%)
1982	701	6.4	6.4
1983	754	7.0	13.4
1984	733	6.7	20.1
1985	828	7.6	27.7
1986	823	7.6	35.3
1987	959	8.8	44.1
1988	966	8.9	53.0
1989	999	9.2	62.2
1990	922	8.5	70.7
1991	997	9.2	79.9
1992	1051	9.7	89.6
1993	1132	10.4	100.0
Total	10865	100.0	100.0

## 2-4. Breast cancer by stage

Table 2-2 demonstrates the distribution of stage at the time of presentation in women with breast cancer in this study. About 9% of the patients did not have stage recorded.

**Table 2-2.** Distribution of stage in women with breast cancer diagnosed between 1982 and 1993.

Stage	Frequency	Percent
1	3469	31.9
2	4230	38.9
3	1504	13.9
4	698	6.4
Unknown	964	8.9
Total	10865	100.0

## 2-5. Breast cancer by grade

Table 2-3 shows the cases by histological grade. As the overwhelming majority had grade unrecorded, this was omitted from the primary survival analysis, but see chapter 5.

**Table 2-3:** Distribution of grade in women with breast cancer, diagnosed in East Anglian Cancer Registry between 1982 and 1993.

Grade	Frequency	Percent
1	293	2.6
2	665	6.1
3	615	5.7
Unknown	9292	85.6
Total	10865	100.0

## 2-6. Breast cancer by morphology

Breast cancer classified by morphological type is shown in table 2-4.

This variable is of limited use since 16% are classified as adenocarcinoma not otherwise specified, and 27% as “others”. Since most tumour series comprise of 70-80% ductal carcinoma, we might speculate that the majority of adenocarcinoma and others are of ductal type, but we cannot be certain.

**Table 2-4:** Frequency of morphology in women with breast cancer, diagnosed between 1982-1993

Morphology	Frequency	Percent
Ductal	4454	41.0
Medulary	154	1.4
Lobular	1314	12.0
Mucinus & Tubular	298	2.8
Adenocarcinoma	1716	15.8
Others	2929	27.0
Total	10865	100.0

## 2-7. Breast cancer by age group

The patients were grouped into five categories of age at diagnosis which are shown in table 2-5. As expected, the older age groups dominate, and breast cancer diagnosed under age 40 was rare.

**Table 2-5:** Distribution of women with breast cancer by different group of age, diagnosed between 1982-1993

Age group	Frequency	Percent
<40	635	5.8
40-49	1767	16.3
50-59	2211	20.3
60-69	2743	25.3
>70	3509	32.3
Total	10865	100.0



## 2-8. Breast cancer by social class

Table 2-6 shows the frequency of social class based on patient occupation in the present study. More than 61% of patients in the database had no information on occupation. For this reason, social class was dichotomised to non-manual (I-II-IIIN) and manual (IIIM-IV-V) in analyses below.

**Table 2-6:** Distribution of social class in women with breast cancer, diagnosed between 1982 and 1993.

Occupation	Frequency	Percent
I	59	0.5
II	1106	10.2
IIIN	1823	16.8
IIIM	294	2.7
IV	567	5.2
V	295	2.7
Not known	6721	61.9
Total	10865	100.0

## 2-9. Breast cancer by deprivation

**Table 2-7:** Distribution of deprivation category in women with breast cancer

diagnosed between 1982 and 1993.

Deprivation	Frequency	Percent
1 (Affluent)	2529	23.3
2	2983	27.4
3	2788	25.7
4	1904	17.5
5 (deprived)	661	6.1
Total	10865	100.0

Table 2-7 shows the cases subdivided by deprivation category, as determined by area of residence using the Carstairs index (Carstairs and Morris, 1989). Note that this is complete for all subjects, since all that is required to categorise a subject is her postcode of residence.

## 2-10. Breast cancer by hospital

**Table 2-8:** Distribution of breast cancer in four major hospitals in East Anglia Region, 1982-1993.

Hospital	Frequency	Percent
Addenbrooke's	5301	48.8
Norfolk & Norwich	3147	29.0
Ipswich	2097	19.2
West Suffolk	320	3.0
Total	10865	100.0

Table 2-8 shows the hospital of diagnosis for the 10865 cases. The majority were diagnosed in the two large general hospitals, Addenbrooke's hospital, Cambridge and the Norfolk and Norwich hospital.

## 2-11. vital status and prognostic variables

Here we tabulate the major variables of interest by whether the subject was alive or dead (from any cause) at follow up. This is not for purposes of formal inference, but to describe the basic data available for analysis. Formal inference about the effects of the various factors on survival will take into account time to death, and will be presented in chapter 4.

Table 2-9 shows deprivation category by vital status. Table 2-10 shows the corresponding table for social class. Both support an association of death with lower SES.

**Table 2-9:** Frequency of breast cancer diagnosed between 1982 and 1993, by Carstairs deprivation index and vital status.

Carstairs deprivation index	Frequency		Alive		Died	
	No.	%	No.	%	No.	%
1 (Affluent)	2529	23.3	1133	44.80	1396	55.20
2	2983	27.4	1280	42.90	1703	57.10
3	2788	25.7	1148	41.17	1640	58.83
4	1904	17.5	773	40.59	1131	59.41
5 (deprived)	661	6.1	242	36.61	419	63.39
Total	10865	(100)	4576	42.11	6289	57.89

**Table 2-10:** Frequency of social class in women with breast cancer by vital status, diagnosed between 1982 and 1993.

Social class	Total		Alive		Died	
	No.	%	No.	%	No.	%
High	2988	72.10	1559	52.17	1429	44.83
Low	1156	27.90	450	38.92	706	61.08
Total	4144	100	2009	48.47	2135	51.53

Table 2-11 shows vital status by morphology. There appears to be a positive association of the adenocarcinoma and “others” categories with death. Table 2-12 shows vital status by age at diagnosis, showing as one might expect a positive correlation of death with older age.

Table 2-13 shows vital status by stage, with deaths tending to occur in the more advanced stage, as expected. The corresponding data for histological grade are shown in table 2-14, with an association of grade 3 with a higher proportion of deaths.

**Table 2-11:** Frequency of morphology of breast cancer by vital status, diagnosed between 1982-1993

Morphology	Total		Alive		Died	
	No	%	No	%	No	%
Ductal	4454	40.99	2418	54.28	2036	45.72
Medulary	154	1.41	90	58.44	64	41.56
Lobular	1314	12.09	642	48.55	672	51.15
Mucinos/Tubular	298	2.74	203	68.12	95	31.88
Adenocarcinoma	1716	15.79	627	36.53	1089	63.47
Others	2929	26.95	596	20.34	2333	79.66
Total	10865	100.00	4576	42.11	6289	57.89

**Table 2-12:** Frequency of patients by age showing the total in each age-group, concerning the number of dead and alive.

Age group	Total		Alive		Died	
	No.	%	No.	%	No.	%
<40	635	5.84	326	51.33	309	48.67
40-49	1767	16.24	1028	58.17	739	41.83
50-59	2211	20.35	1270	57.44	941	42.56
60-69	2742	25.24	1287	46.93	1456	53.07
+70	3509	32.30	665	18.95	2844	81.05
Total	10865	100	4576	42.11	6289	57.89

**Table 2-13:** Vital status by stage in women with breast cancer- diagnosed between 1982 and 1993.

Stage	Total		Alive		Died	
	No	%	No	%	No	%
1	3469	23.74	2351	67.77	1118	32.23
2	4230	18.74	1856	43.87	2365	56.13
3	1504	2.44	242	16.09	1262	83.91
4	689	0.28	28	4.06	670	95.94
Total	9901	100	4486	45.30	5415	54.70

**Table 2-14:** Frequency of grade in women with breast cancer by vital status, diagnosed between 1982-1993

Grade	Total		Alive		Died	
	No	%	No	%	No	%
1	293	18.63	242	82.54	51	17.41
2	665	42.28	432	64.96	233	35.04
3	615	39.10	335	54.47	280	45.53
Total	1573	100.00	1009	64.14	564	35.86

## **2-12. Variables used in survival analysis**

The major variables for survival analysis are age, social class (non-manual and manual), deprivation (5 categories), disease stage and morphological type. Due to the small number with known grade, this will not be part of the main survival analysis, although we shall consider it in detail in chapter 5. The major target of the analysis is to estimate the extent to which stage and morphology account for the effect of social class and deprivation.



# CHAPTER 3

## 3. Relationship between socioeconomic status and other variables

### 3-1. Introduction

In this chapter, the joint distribution of the 10865 women with breast cancer diagnosed between 1982 and 1993, by SES and tumour attributes will be examined. This will establish for example, whether or not women with low SES present with tumours at a more advanced stage.

### 3-2. Social class

Table 3-1 shows the cross-tabulation of disease stage and social class. Women in the low (manual) social class tend to have worse stage at presentation. This is statistically significant ( $p < 0.001$ ).

Table 3-2 shows the distribution of histological grade by social class. Although there are higher proportions of low social class women with grade 2 and 3, this does not reach statistical significance. It should be noted, however, that less than 10% of the cases have grade recorded.

Table 3-3 shows the cross-tabulation of morphology by social class. The lower social class women have slightly lower rates of ductal carcinoma and slightly higher rates of adenocarcinoma not otherwise specified and “others” ( $p < 0.001$ ). This may be due to treatment in centres with less specialised pathology laboratories rather than a biological effect.

Table 3-4 shows social class by age at diagnosis. The low social class cases are slightly older, but this is not significant. Table 3-5 shows social class by hospital. A greater proportion of lower social class women was observed in the Norfolk and Norwich and Ipswich hospitals, but this was not significant.

**Table 3-1:** Distribution of stage by social class in women with breast cancer, diagnosed between 1982 and 1993.

Stage	Social class					
	High		Low		Total	
	No	(%)	No	(%)	No	(%)
1	1156	(40.2)	377	(34.4)	1533	(38.6)
2	1257	(43.8)	468	(42.7)	1725	(43.5)
3	302	(10.5)	163	(14.9)	465	(11.7)
4	157	(5.5)	87	(7.9)	244	(6.2)
Total	2872	(100)	1095	(100)	3967	(100)

**Table 3-2:** Distribution of grade by social class in women with breast cancer, diagnosed between 1982 and 1993, EACR.

Grade	Social class		
	High	Low	Total
	No (%)	No (%)	No (%)
1	117 (18.6)	26 (12.4)	143 (17.1)
2	262 (41.7)	91 (43.6)	353 (42.1)
3	250 (39.7)	92 (44.0)	342 (40.8)
Total	629 (100.0)	209 (100.0)	838 (100.0)

**Table 3-3:** Distribution of morphology by social class in women with breast cancer, diagnosed between 1982 and 1993, EACR

Morphology	Social class				Total	
	High		Low			
	No	(%)	No	(%)	No	(%)
Ductal	1524	(51.0)	525	(45.4)	2049	(49.4)
Medulary	52	(1.7)	21	(1.8)	73	(1.8)
Mucinus & Tubular	411	(13.8)	136	(11.8)	547	(13.2)
Lobular	87	(2.9)	29	(2.5)	116	(2.8)
Adenocarcinoma	400	(13.4)	165	(14.3)	565	(13.6)
Others	514	(17.2)	280	(24.2)	794	(19.2)
Total	2988	(100)	1156	(100)	4144	(100)

**Table 3-4:** Distribution of age group by social class in women with breast cancer, diagnosed between 1982 and 1993, EACR.

Age group	Social class		Total
	High	Low	
	No (%)	No (%)	No (%)
<40	249 (8.3)	86 (7.4)	335 (8.1)
40-49	732 (24.5)	263 (22.8)	995 (24.0)
50-59	759 (25.4)	296 (25.6)	1055 (25.4)
60-69	691 (23.1)	256 (22.2)	947 (22.9)
+70	557 (18.7)	255 (22.0)	812 (19.6)
Total	2988 (100.0)	1156 (100.0)	4144 (100.0)

**Table 3-5:** Distribution of social class by hospital in women with breast cancer diagnosed between 1982 and 1993.

Social class	Hospital				
	Addenbrooke's	Norfolk/Norwich	Ipswich	West Suffolk	Total
	No (%)	No (%)	No (%)	No (%)	No (%)
High	1802 (73)	698 (71)	419 (70)	69 (77)	2988 (72)
Low	661 (27)	291 (29)	183 (30)	21 (23)	1156 (28)
Total	2463 (100)	989 (100)	602 (100)	90 (100)	4144 (100)

### 3-3. Deprivation

**Table 3-6:** Distribution of stage by deprivation in women with breast cancer diagnosed between 1982 and 1993.

Stage	Deprivation					Total
	1(Affluent)	2	3	4	5 (Deprived)	
	No (%)	No (%)	No (%)	No (%)	No (%)	
1	856 (36.9)	962 (35.3)	863 (34.4)	587 (33.8)	201 (33.3)	3469 (35.0)
2	988 (42.7)	1173 (43.0)	1066 (42.4)	750 (43.1)	253 (42.0)	4230 (42.7)
3	345 (14.7)	406 (14.9)	396 (15.8)	270 (15.5)	87 (14.4)	1504 (15.2)
4	132 (5.7)	186 (6.8)	186 (7.4)	132 (7.6)	62 (10.3)	698 (7.1)
Total	2321 (100)	2727 (100)	2511 (100)	1739 (100)	603 (100)	9901 (100)

Table 3-6 shows deprivation category by disease stage. The more deprived categories are more likely to present with stage 3 or 4 tumours ( $p=0.048$ ). The corresponding tabulation for histological grade is shown in table 3-7. There is a slight tendency to a small proportion of grade 1 tumours in the most deprived category, but this is not significant. Again, however, there are relatively few cases with grade recorded (14%).

Table 3-8 shows deprivation by morphological type. The more deprived categories tend to have lower proportions of ductal carcinoma and higher proportions of adenocarcinoma and “others” ( $p<0.001$ ). This may reflect centre of diagnosis or treatment.

Table 3-9 shows deprivation category by age at diagnosis. There was a significant association ( $p < 0.001$ ) with the more affluent cases tending to be younger.

Table 3-10 shows deprivation category by hospital. There was a significant association, with the small West Suffolk hospital having a higher proportion of more deprived women.



**Table 3-7:** Distribution of grade by deprivation in women with breast cancer diagnosed between 1982 and 1993.

Grade	Deprivation					Total
	1 (affluent)	2	3	4	5(deprived)	
	No (%)	No (%)	No (%)	No (%)	No (%)	
1	72 (19.1)	82 (19.0)	69 (18.5)	55 (18.5)	15 (16.1)	293 (18.6)
2	140 (37.0)	195 (45.3)	164 (44.0)	129 (43.3)	37 (39.8)	665 (42.3)
3	166 (43.9)	154 (35.7)	140 (37.5)	114 (38.2)	41 (44.1)	615 (39.1)
Total	378 (100)	431 (100)	373 (100)	298 (100)	93 (100)	1573 (100)

**Table 3-8:** Distribution of morphology by deprivation in women with breast cancer diagnosed between 1982 and 1993, EACR.

Morphology	Deprivation					Total
	1 (affluent)	2	3	4	5 (deprived)	
	No (%)	No (%)	No (%)	No (%)	No (%)	
Ductal	1121 (44.3)	1237 (41.5)	1087 (39.0)	762 (40.0)	247 (37.4)	4454 (41.0)
Medulary	42 (1.2)	37 (1.2)	34 (1.2)	32 (1.7)	9 (1.4)	154 (1.4)
Lobular	320 (12.6)	352 (11.8)	319 (11.4)	241 (12.7)	82 (12.4)	1314 (12.1)
Mucinus/ Tubular	67 (2.6)	82 (2.7)	66 (2.4)	68 (3.6)	15 (2.3)	298 (2.7)
Adenocarcinoma	361 (14.3)	469 (15.7)	464 (16.6)	299 (15.7)	123 (18.6)	1716 (15.8)
Others	618 (24.4)	806 (27.0)	818 (29.3)	502 (26.4)	185 (28.0)	2929 (27.0)
Total	2529	2983	2788	1904	661	10865 (100)

**Table 3-9:** Distribution of Age group by deprivation in women with breast cancer diagnosed between 1982 and 1993.

Age group	Deprivation					Total
	1 (Affluent)	2	3	4	5 (Deprived)	
	No %	No %	No %	No %	No %	
<40	179 (7)	170 (6)	166 (6)	85 (4)	35 (5)	635 (6)
40-49	454 (18)	519 (17)	424 (15)	284 (15)	86 (13)	1767 (16)
50-59	545 (22)	576 (19)	545 (20)	395 (21)	150 (23)	2211 (20)
60-69	610 (24)	761 (26)	717 (26)	463 (24)	192 (29)	2743 (25)
+70	741 (29)	957 (32)	936 (33)	677 (36)	198 (30)	3509 (33)
Total	2529 (100)	2983 (100)	2788 (100)	1904 (100)	661 (100)	10865 (100)

**Table 3-10:** Distribution of deprivation by hospital in women with breast cancer diagnosed between 1982 and 1993.

Deprivation	Hospital				
	Addenbrooke's	Norfolk/Norwich	Ipswich	West Suffolk	Total
	No (%)	No (%)	No (%)	No (%)	No (%)
1 (Affluent)	1268 (24)	677 (21)	516 (27)	68 (21)	2529 (23)
2	1385 (26)	947 (30)	561 (27)	90 (8)	2983 (27)
3	1330 (25)	806 (26)	571 (27)	81 (25)	2788 (26)
4	971 (18)	534 (17)	328 (16)	71 (22)	1904 (18)
5 (Deprived)	347 (7)	183 (6)	121 (3)	10 (4)	661 (6)
Total	5301 (100)	3147 (100)	2097 (100)	320 (100)	10865 (100)

### 3-4. Analysis of the two indices of SES

Table 3-11 shows social class tabulated by deprivation category. As one would expect, there is a clear and strong relationship between the two factors ( $p < 0.001$ ). In the most affluent category, only 18% were in the lower social class, whereas 49% of the most deprived were in the lower social class.

**Table 3-11:** Distribution of social class by deprivation in women with breast cancer diagnosed between 1982 and 1993.

Social class	Deprivation					Total
	1(Affluent)	2	3	4	5(Deprived)	
	No (%)	No (%)	No (%)	No (%)	No (%)	
High	852 (82.2)	842 (76.0)	708 (69.3)	448 (63.4)	138 (51.0)	2988 (72.1)
Low	185 (17.8)	265 (24.0)	314 (30.7)	259 (36.6)	133 (49.0)	1156 (27.9)
Total	1037 (100)	1107 (100)	1022 (100)	707 (100.0)	271 (100.0)	4144 (100)

### 3-5. Discussion

Arguably the most important results in this chapter relate to the significant associations of disease stage with social class and disease stage with deprivation category. For either measure, low socioeconomic status was significantly associated with more advanced stage of breast cancer at presentation. This suggests that at least some of the poorer survival of low socioeconomic status breast cancer patients, which has been observed in the past, may be

attributable to later diagnosis and therefore poorer stage. The joint effects on survival will be examined in the next chapter. There were also significant associations of morphological type with social class and with deprivation category, but these were mainly due to more tumours in the low socioeconomic status cases falling into the less specific categories (adenocarcinoma not otherwise specified and 'other'), rather than to particular types associated with poorer prognosis.

# CHAPTER 4

## 4. Survival Analysis (excluding grade)

### 4-1. Introduction

This chapter gives the main results of this thesis. We report the effects of social class and deprivation category on survival, both for breast cancer deaths and for all causes. We give the estimates both unadjusted and adjusted for stage and morphology, to show the extent to which the effect of socioeconomic status on survival can be attributed to stage at diagnosis on type of tumour. The degree to which the socioeconomic effects can be attributed to stage or morphology is quantified using the estimate of Freedman et al (1992) as follows: if  $HR_U$  is the hazard ratio for social class adjusted only for age and  $HR_A$  is the hazard ratio adjusted for both age and stage, the percentage of the age-adjusted social class effect which is attributable to confounding with stage is

$$100 \left\{ 1 - \frac{\log(HR_A)}{\log(HR_U)} \right\}$$

Thus, if the adjusted and unadjusted hazard ratios were exactly equal (i.e. adjusting for stage made no difference to the estimate at all), then the percentage attributable would be 0%. If on

the other hand, the adjusted hazard ratio was 1.0 (i.e., no effect of social class whatever after adjusting for stage), the estimate would be 100% of the effect attributable to stage.



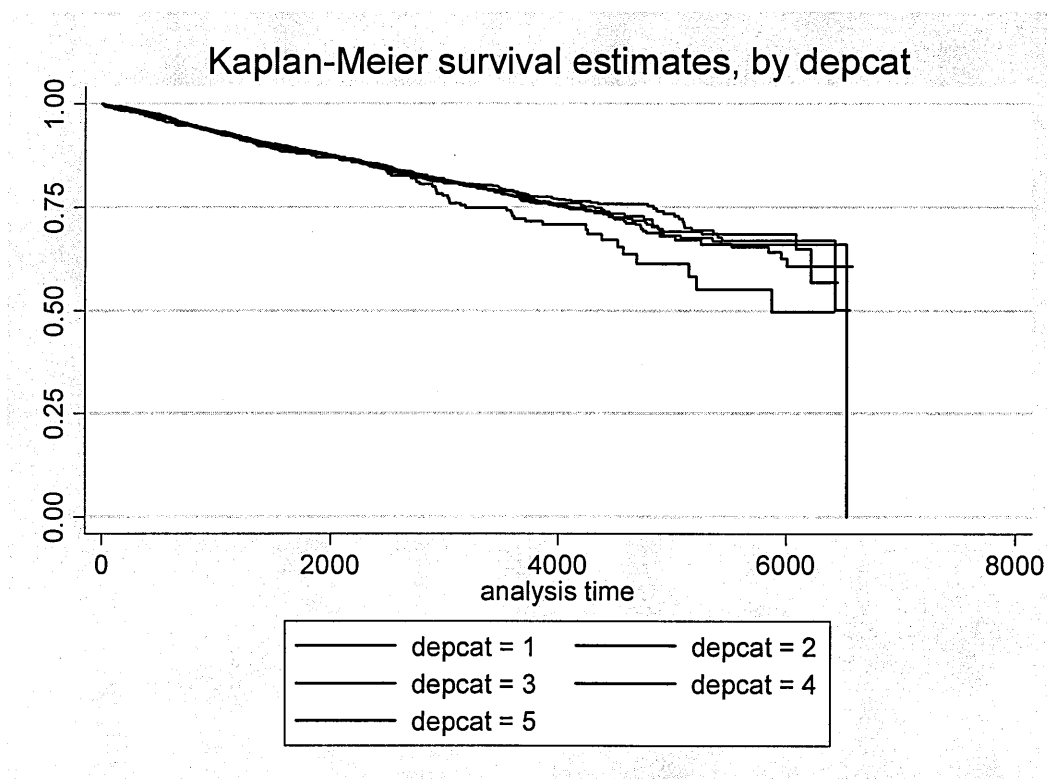
## 4-2. Univariate and age-adjusted analysis

In this section we report univariate analyses. In order to examine the crude effects of each individual risk factor, we show survival curves using Kaplan-Meier survival estimates. We also show age-adjusted relative hazards from proportional hazards regression modelling.

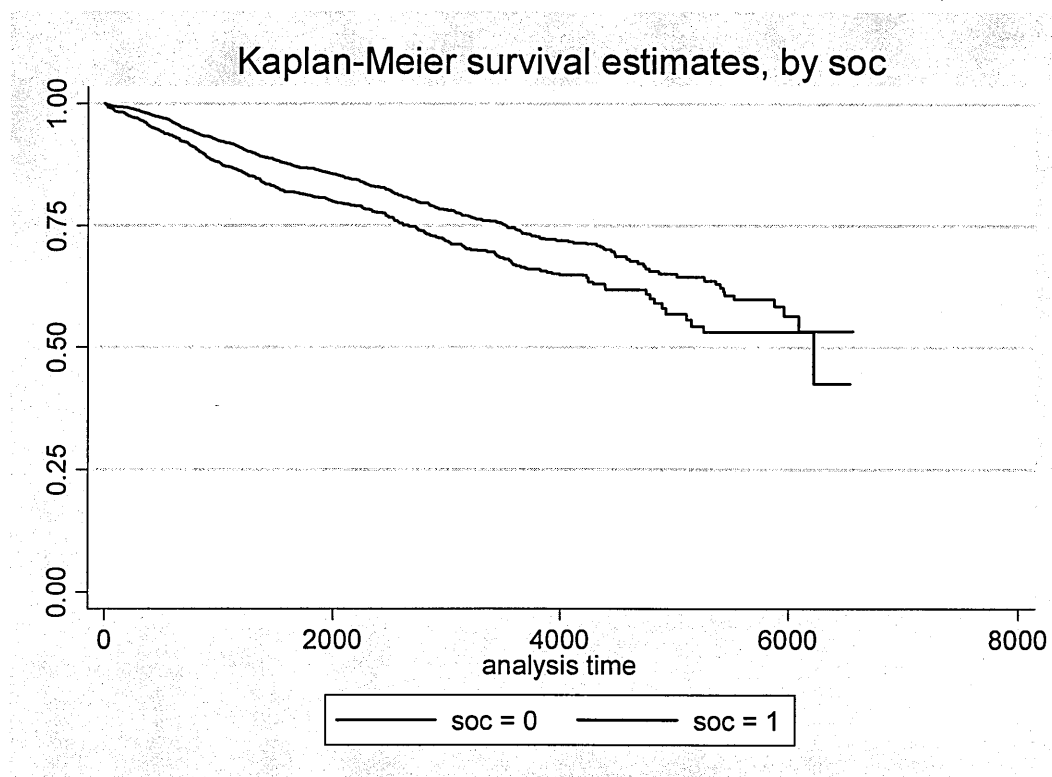
Table 4-1 allows a first glance at the data, in terms of age-adjusted relative hazard estimates of breast cancer death for the main explanatory variables and of simple 5-year survival probability comparisons. For each category of each of five explanatory variables, the table reports the total number of cases in the category (column 3), the number of cases in this category who died of breast cancer (column 4), the 5-year survival probability with corresponding 95% confidence interval (columns 5-6), and the estimated age-adjusted hazard ratio and its corresponding 95% confidence interval. A separate proportional hazards analysis was performed for each of the five variables to estimate the hazard ratios for the corresponding categories. The analysis did not acknowledge the ordinal nature of the variables stage, grade and deprivation, as these variables were treated as categorical factors. Table 4-2 shows the corresponding results for deaths from all causes among breast cancer cases.

Survival curves (breast cancer deaths only) for deprivation category, social class and stage are shown in Figures 4-1 to 4-3. Interestingly, for deprivation category, the differences in survival only emerge after around six years, suggesting a possible treatment effect.

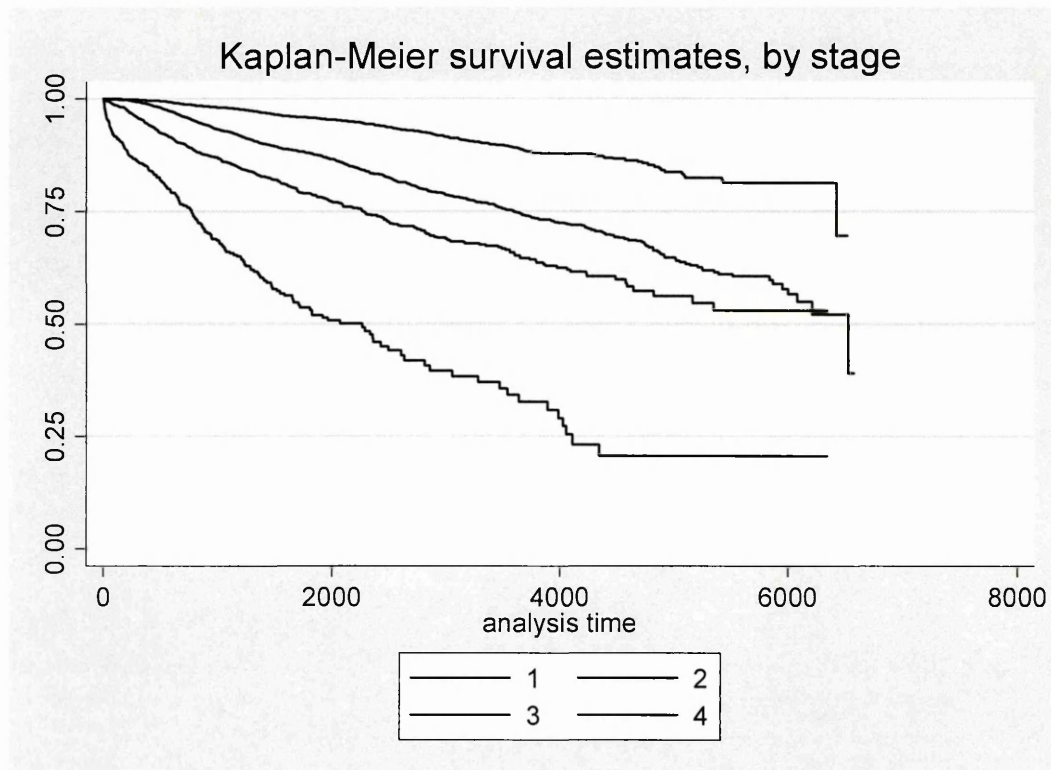
**Figure 4-1:** Survival (breast cancer deaths only, x-axis is in days) by deprivation category



**Figure 4-2:** Survival (breast cancer deaths only, x-axis is in days) by social class



**Figure 4-3:** Survival (breast cancer deaths only, x-axis is in days) by stage at presentation



**Table 4-1:** Basic data and age-adjusted estimates of survival effects by univariate analysis  
(breast cancer deaths only)

Factors	Category	No. of cases	No. of deaths <sup>a</sup>	5-year survival probability	(95% CI )	Haz. Ratio	(95% CI)
<b>Stage</b>	1	3469	260	0.96	0.95-0.97	1.00	---
	2	4230	651	0.91	0.89-0.92	2.40	2.07-2.78
	3	1504	237	0.89	0.81-0.87	3.56	2.97-4.26
	4	698	142	0.62	0.55-0.69	11.31	9.17-13.93
<b>Grade</b>	1	293	12	0.98	0.94-0.99	1.00	---
	2	665	103	0.89	0.85-0.91	4.08	2.24-7.42
	3	615	169	0.79	0.75-0.83	7.27	4.04-13.08
<b>Morphology</b>	Ductal	4454	605	0.90	0.89-0.92	1.00	---
	Medulary	154	15	0.93	0.86-0.97	0.63	0.37-1.05
	Lobular	1314	205	0.91	0.89-0.93	1.12	0.95-1.31
	Mucinus/tubular	298	15	0.99	0.96-1.00	0.30	0.18-0.52
	Adenocarcinoma	1716	186	0.95	0.93-0.97	0.67	0.56-0.79
	Others	2929	357	0.88	0.86-0.90	1.08	0.94-1.25
<b>Social class</b>	High	2988	448	0.90	0.88-0.91	1.00	---
	Low	1156	240	0.86	0.83-0.88	1.32	1.12-1.55
<b>Deprivation</b>	Most affluent	2529	320	0.91	0.89-0.92	1.00	---
	2	2983	376	0.91	0.90-0.93	1.01	0.87-1.18
	3	2788	357	0.91	0.89-0.93	1.02	0.87-1.19
	4	1904	240	0.91	0.89-0.93	1.00	0.84-1.18
	Most deprived	661	90	0.91	0.88-0.94	1.21	0.95-1.54

<sup>a</sup> Underlying cause.

**Table 4-2:** Basic data and age-adjusted estimates of survival effects by univariate analysis for all causes of deaths.

Factors	Category	No. of cases	No. of deaths <sup>a</sup>	5-year survival probability	(95% CI )	Haz. Ratio	(95% CI)
<b>Stage</b>	1	3469	530	0.84	0.83-0.86	1.00	---
	2	4230	1370	0.67	0.65-0.69	2.05	1.91-2.21
	3	1504	933	0.37	0.35-0.41	4.52	4.17-4.91
	4	698	606	0.13	0.10-0.16	11.40	10.34-12.57
<b>Grade</b>	1	293	20	0.92	0.89-0.96	1.00	---
	2	665	130	0.79	0.76-0.83	2.15	1.59-2.92
	3	615	174	0.71	0.67-0.75	2.62	1.94-3.54
<b>Morphology</b>	Ductal	4454	1281	0.70	0.69-0.73	1.00	---
	Medulary	154	33	0.71	0.63-0.78	0.80	0.63-1.04
	Lobular	1314	376	0.71	0.68-0.74	1.11	1.02-1.22
	Mucinus/tubular	298	36	0.87	0.83-0.91	0.59	0.48-0.74
	Adenocarcinoma	1716	645	0.62	0.59-0.65	1.31	1.22-1.42
	Others	2929	1724	0.40	0.39-0.43	2.34	2.20-2.49
<b>Social class</b>	High	2988	892	0.69	0.68-0.72	1.00	---
	Low	1156	409	0.64	0.61-0.68	1.20	1.09-1.32
<b>Deprivation</b>	Most affluent	2529	906	0.63	0.61-0.66	1.00	---
	2	2983	1117	0.62	0.60-0.64	1.06	0.99-1.15
	3	2788	1067	0.61	0.59-0.64	1.10	1.02-1.19
	4	1904	729	0.61	0.59-0.64	1.10	1.02-1.20
	Most deprived	661	286	0.56	0.52-0.61	1.24	1.11-1.39

<sup>a</sup>All causes.

Note that in Tables 4-1 and 4-2 significant and clinically important effects are associated with advanced tumour stage. In particular, the 11.3 and 11.4 estimates for the hazard ratio associated with stage 4 shows, as expecting that a patient from the population of stage 4 cases is expected to have a more than 10-fold risk of dying of breast cancer or other causes when compared with that of a woman from the stage 1 cases. The results in these tables also support the hypothesis of a significant effect of grade upon hazard of breast cancer death. The estimated hazard ratios for the morphology variable for breast cancer deaths only indicate poorest survival for ductal, lobular and “others” types. For deaths from any cause, the results suggest an increased hazard associated with the “others” category and a moderate but significant increased associated with adenocarcinoma. There is also significant evidence of a risk decrease associated with mucinus/tubular morphology for breast cancer death and all causes deaths.

The estimated hazard ratios for social class are 1.32 and 1.20 for breast cancer and all causes deaths respectively, both significant. This suggests that a patient of low socioeconomic status will have a risk of dying during the follow-up period which is 20-32% higher than a patient of high socioeconomic status. Of all the categories of deprivation, only the most deprived one appears to be associated with a statistically significant or suggestive effect on fatality.

The initial main question addressed by this project is the extent to which the significant effects associated in a univariate analysis with deprivation and social class are attributable to differences in the conditions of the tumour at diagnosis, as represented by stage and morphology (results for grade follow in the next chapter). The results reported in tables 4-3, 4-4, 4-5, 4-6, 4-7 and 4-8 are relevant to this question.

### 4-3. Adjusted effects - basic results

Consider first Table 4-3 for all deaths, which reports estimated hazard ratios and corresponding 95% confidence intervals for the four non-reference categories of the variable deprivation, calculated by adjusting for stage and age. These estimates have been calculated without distinguishing between those death events which are clearly related to breast cancer and those which are not. The results in this part show that adjusting for stage does change the point value and the confidence interval of the hazard ratio estimates but the most deprived category still has a significantly higher HR than the least. An interpretation of this finding is that the apparent hazard disadvantage of women in the most deprived category can be partly but not completely explained in terms of a poorer stage of the tumour at diagnosis.

Table 4-3 for breast cancer deaths only reports estimated hazard ratios and corresponding 95% confidence intervals associated with the deprivation categories, again adjusting for stage and age, focusing on only those death events which are clearly related to breast cancer, that is, treating all other deaths as censoring events. The hazard ratio estimates in this section of the table are not substantially different from those of all causes of death, in terms of point estimates, although their corresponding confidence intervals are much larger. The latter fact can be interpreted to be an effect of the higher degree of censoring and fewer events due to discarding non-breast-cancer deaths, with a consequent loss of statistical power. The hazard ratio for the most deprived category is augmented rather than attenuated by adjustment for stage.

**Table 4-3: Deprivation effect on survival adjusted for age and stage**

Deprivation	All deaths		Breast cancer deaths	
	H.R.	(95% CI)	H.R.	(95% CI)
Most affluent	1.00	---	1.00	---
2	1.05	0.98-1.14	1.04	0.89-1.22
3	1.01	0.94-1.09	1.01	0.86-1.19
4	1.02	0.94-1.11	0.98	0.82-1.17
Most deprived	1.16	1.03-1.31	1.23	0.96-1.55

Table 4-4 shows hazard ratio estimates for the deprivation categories adjusting for age and morphology, taking all deaths as endpoints in the first part of table and then breast cancer deaths only in the second. The results in this table show that adjusting for morphology for either endpoint does not change point and interval hazard ratio estimates substantially. In particular, the hazard ratio associated with the most deprived category does not appear to be substantially modified by the adjusting, neither in point estimate nor in interval. This suggests that the apparent hazard disadvantage of women in the most deprived category cannot be explained in terms of a more unfavourable morphology of the tumour at diagnosis. Confidence intervals on the breast cancer deaths estimates are wider than the corresponding ones in the all deaths part of the table as before.



**Table 4-4:** Deprivation effect on survival adjusted for age and morphology

Deprivation categories	All deaths		Breast cancer deaths	
	HR	(95% CI)	H.R.	(95% CI)
Most affluent	1.00	---	1.00	---
2	1.02	0.95-1.10	1.02	0.87-1.19
3	1.02	0.95-1.09	1.03	0.88-1.20
4	1.02	0.95-1.11	1.00	0.85-1.21
Most deprived	1.24	1.11-1.38	1.23	0.96-1.55

Table 4-5 shows the estimated hazard ratio for low social class, adjusting for age and stage, using all deaths as failure events and breast cancer deaths separately, as before. Interestingly, a comparison of Tables 4-2 and table 4-5, all deaths section, shows that adjusting for stage causes a substantial reduction in the estimated hazard ratio, making it practically indistinguishable from its null value 1. This finding would seem to suggest that when all deaths are considered the hazard disadvantage of lower social class women is to a great extent explained as being a consequence of a more advanced stage of the tumour at diagnosis. The second part of table 4-5 reports the estimated hazard ratio associated with a lower social class, after adjusting for age and stage, taking only those deaths which were clearly related to breast cancer as failure events. The results in this part of table show that, unlike in the all deaths analysis, adjusting for stage causes a considerably smaller reduction in the estimated hazard ratio associated with social class. The latter remains significant after adjustment. A possible

combined interpretation of the results of Table 4-5 is the following: a higher tumour stage at diagnosis might well explain the disadvantage of lower social class women in terms of the overall death rate, but to a lesser extent their disadvantage in terms of that component of the hazard of death which is strictly related to breast cancer. This finding needs further research to confirm and clarify it.

**Table 4-5:** Effect of social class on survival after adjusting for age and stage

Social class	All deaths		Breast cancer deaths	
	H.R.	(95% CI)	H.R.	(95% CI)
High	1.00	---	1.00	---
Low	1.07	0.97-1.18	1.22	1.03-1.44

**Table 4-6:** Effect of social class on survival after adjusting for age and morphology.

Social class	All deaths		Breast cancer deaths	
	H.R.	(95% CI)	H.R.	(95% CI)
High	1.00	---	1.00	---
Low	1.19	1.09-1.31	1.31	1.12-1.54

Table 4-6 shows the hazard ratio estimates for the social class categories adjusting for age and morphology. The result in this table suggest that the apparent hazard disadvantage of women in low social class cannot be substantially explained in term of more unfavourable

morphology of tumour at the time of presentation. This is particularly so when analysis is restricted to breast cancer deaths.

It should be noted that adjusting for both stage and morphology simultaneously does not change the odds ratios markedly from those adjusted for stage alone. This is the case for both measures of socioeconomic status and both death endpoints.

#### **4-4. Adjusted effects- summary and implications**

To draw together the adjusted and unadjusted effects, see Table 4.7. In this table the unadjusted and adjusted hazard ratios for low social class and the most deprived category are shown, by death endpoint and adjusting variable. It can be seen clearly that morphological type does not account for a substantial proportion of the effect of either socioeconomic measure on either death endpoint. Stage, interestingly, accounts for some of the effect of social class on hazard of breast cancer death and all deaths, but only accounts for a proportion of the deprivation effect on all deaths.

The corresponding Freedman statistics for the percentage explained are shown in Table 4-8. The table shows that stage accounts for around 31-63% of the effect of socio-economic status on survival to death from all causes, and 0-28% of the effect on survival to death from breast cancer specifically. Morphology does not substantially explain any socioeconomic effects on survival. It is interesting that the percentage effect explained by stage is greater for social class than for area-based deprivation category. This suggests that there are aspects of socioeconomic status which bear on the survival of breast cancer patients which are

encompassed by the deprivation category but not by social class (which is based on occupation alone).

Another interesting point is the fact that stage accounts for a greater proportion of the effect of socioeconomic status on all-cause deaths than on breast cancer deaths specifically. It is not clear why this should be so. It is understandable that breast cancer patients of lower socioeconomic status have higher death rates from whatever cause, due to the general association of poverty with ill-health, but it is less clear why stage of breast cancer should account for some of the deaths from other causes than breast cancer. Possible explanations are:

- (1) misclassification of cause of death, in that some deaths from other causes may be due at least in part to the breast cancer;
- (2) there may be some deaths occurring as a result of more aggressive treatments administered to advanced stage patients, which are not classified as breast cancer deaths; or
- (3) Confounding of stage of disease with other aspects of low socioeconomic status which contribute to an increased overall mortality rate.

Disentangling these is a target for future research.

**Table 4-7:** Adjusted and unadjusted effects of socioeconomic status, stratified by death endpoint (breast cancer or all causes), measure of socioeconomic status (social class or deprivation category) and adjusting variable (stage or morphology).

Socioeconomic status variable	Adjusting variable	Adjusted?	All deaths		Breast cancer deaths	
			H.R.	(95% CI)	H.R.	(95% CI)
Social class	Stage	No	1.20	(1.09-1.32)	1.32	(1.12-1.55)
		Yes	1.07	(0.97-1.18)	1.22	(1.03-1.44)
Social class	Morphology	No	1.20	(1.09-1.32)	1.32	(1.12-1.55)
		Yes	1.19	(1.09-1.31)	1.31	(1.12-1.54)
Deprivation	Stage	No	1.24	(1.11-1.39)	1.21	(0.95-1.54)
		Yes	1.16	(1.03-1.31)	1.23	(0.96-1.55)
Deprivation	Morphology	No	1.24	(1.11-1.39)	1.21	(0.95-1.54)
		Yes	1.24	(1.11-1.38)	1.23	(0.95-1.55)

**Table 4-8:** Freedman estimates of the percentages of effects of socioeconomic status explained by stage and morphological type, stratified by death endpoint (breast cancer or all causes).

Socioeconomic status measure	Adjusting variable	% explained	
		All cause deaths	Breast cancer deaths
Social class	Stage	63%	28%
Social class	Morphology	5%	3%
Deprivation	Stage	31%	0%
Deprivation	Morphology	0%	0%

# CHAPTER 5

## 5. Additional analyses of histological grade data

### 5-1. Additional data

A total of 1573 breast cancer cases diagnosed between 1982 and 1993 had recorded grade. Because of the small numbers with recorded grade, we dispensed with the limits on year of diagnosis and used all data available until 1998. This gave 6199 cases with grade recorded as shown in table 5-1.

**Table 5-1:** Frequency distribution of histological grade, tumour diagnosed in 1982-1998.

Grade	Frequency	Percent
1	1358	22.0
2	2778	44.8
3	2063	33.2
Total	6199	100.00

The distribution of grade in this table using the larger tumour series from the longer time interval (1982-1998) is similar to the proportions observed in the shorter interval of 1982-1993

in table 2-3. One difference is the smaller number of grade 3 cases in the larger series, 33.2% compared to the 40% shown in table 2-3.

The highest proportion of patients presented with grade 2 disease, with 44.8%, while the patients with grade 1 cancers formed the lowest proportion with 22.0%.

**Table 5-2:** Association of grade and social class among women with breast cancer diagnosed between 1982-1998, EACR

Grade	Social class				Total
	High		Low		
	No.	(%)	No.	(%)	
1	309	(19.2)	221	(20.8)	530 (19.9)
2	689	(42.9)	464	(43.8)	1153 (43.2)
3	608	(37.9)	375	(35.4)	983 (36.9)
Total	1606	(100.00)	1060	(100.00)	2666 (100.00)

$\chi^2=2.01$ , 2 d.f., Not Significant

The association between grade and social class (dichotomised as in previous chapters) is shown in Table 5-2. This association was not substantially different from that observed with the smaller sample size. Note that a total of 2666 cases had both social class and grade records. Thus, of those with grade recorded, social class was only available for a minority of cases. This minority may not be representative, so results should be interpreted with caution. A chi-squared comparison showed no significant association between social class and grade. In both the higher and lower social classes, grade 2 cancers were the most frequently observed, with 42.9% and 43.8% respectively.



**Table 5-3:** Association of grade with deprivation among women with breast cancer diagnosed between 1982 and 1998, EACR.

Grade	Deprivation category					Total
	Most affluent	2	3	4	Most deprived	
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	
1	362(22.82)	380(21.90)	356(23.62)	187(18.23)	73 (21.16)	1358(21.91)
2	669(42.18)	808(46.57)	672(44.60)	479(46.67)	150(43.48)	2778(44.81)
3	555(35.00)	547(31.53)	479(31.78)	360(35.10)	122(35.36)	2063(33.28)
Total	1586 (100)	1735(100)	1507(100)	1026(100)	345 (100)	6199 (100)

$\chi^2=19.45$ , 8 d.f.,  $p=0.02$

Table 5-3 shows the association between grade and deprivation. The association was statistically significant, although the absolute magnitude of the differences in grade distribution among deprivation categories was small. The more deprived categories had slightly poorer histological grade than the more affluent.

## 5.2 Survival by grade, social class and deprivation category- death from any cause

Table 5.4 shows the unadjusted effect of histological grade on survival to death from any cause. The effect of grade on survival is very significant, unadjusted for other variables. As one would expect, the results in this table show an increasing risk of death with higher grade. Note that in this larger tumour series, the hazard ratio for grade 3 tumours is larger, at 3.18 compared to 2.62 in table 4-2.

**Table 5-4:** Unadjusted Hazard ratio for histological grade, considering all causes of deaths

Grade	Haz. Ratio	95% Conf. Interval
1	1.00	-
2	1.99	1.63-2.42
3	3.18	2.62-3.85

Table 5-5 shows the unadjusted effect of deprivation category on survival to death from any cause. The effect of deprivation, in terms of the estimated hazard ratios, was not substantially changed by using the larger number of cases. The unadjusted effect of deprivation on survival was significant using all causes of death as the failure event. As before, the major manifestation of the effect is in an increased hazard of death in the most deprived category.

**Table 5-5:** The effect of deprivation (unadjusted) on breast cancer survival, considering all causes of deaths. 1982-1998.

<b>Deprivation</b>	<b>Haz. Ratio</b>	<b>95% Con. Interval</b>
Most affluent	1.00	-
2	1.06	1.00-1.13
3	1.08	1.01-1.15
4	1.11	1.03-1.19
Most deprived	1.26	1.15-1.40

**Table 5-6:** The effect of Social class (unadjusted) on breast cancer survival, considering all causes of deaths. 1982-1998.

<b>Social class</b>	<b>Haz. Ratio</b>	<b>95% Con. Interval</b>
High	1.00	-
Low	1.25	1.16-1.36

Table 5-6 shows the unadjusted effect of social class on survival, taking all cases between 1982 and 1998 and using all causes of death as endpoint. The hazard for the lower social classes is significantly higher than that for the higher classes, as was observed with the smaller tumour series in table 4-2.

**Table 5-7:** The effect of Social class on breast cancer survival, adjusted for grade, considering all causes of deaths. 1982-1998.

<b>Factor / category</b>	<b>Haz. Ratio</b>	<b>95% Conf. Interval</b>
<b>Social class</b>	High	1.00
	Low	1.33
<b>Grade</b>	1	1.00
	2	1.94
	3	3.37

Table 5-7 shows the estimated hazard ratio for lower social classes adjusting for grade, using all deaths as failure events. Interestingly, adjusting for grade has increased the estimated hazard ratio from 1.25 to 1.33. This finding might suggest that when all deaths are considered, the survival disadvantage of lower social class women is increased after adjusting for grade, possibly as a result of negative confounding. On the other hand, the difference between the unadjusted and adjusted hazard ratios is small, so this may be a chance finding.

Table 5-8 shows the hazard ratio estimates for the deprivation categories adjusting for grade. The significance of the effect of deprivation was reduced when adjusted for grade. The hazard ratio for the most deprived category, however, increased when adjusted for grade. The results suggest that the apparent survival disadvantage of women in the most deprived group cannot be explained in terms of tumour grade at diagnosis.

**Table 5-8:** The effect of deprivation (based on residential area) on breast cancer survival, adjusted for grade, considering all causes of deaths. 1982-1998

Factor / category		Haz. Ratio	95% Conf. Interval
Grade	1	1.00	-
	2	1.98	1.62-2.41
	3	3.17	2.61-3.84
Deprivation	Most affluent	1.00	-
	2	1.08	0.92-1.25
	3	1.01	0.86-1.18
	4	1.14	0.96-1.34
	Most deprived	1.49	0.90-1.46

### 5.3. Grade, social class, deprivation category and survival- breast cancer deaths only

Table 5-9 shows the unadjusted effect of grade on survival to death from breast cancer.

A significant effect of grade was observed, with a considerably steeper gradient of risk than was observed using all causes of death as the endpoint. In particular, the estimated hazard ratio of 7.39 associated with grade 3 disease is very striking. Clearly, the use of all causes of death dilutes the effect of histological grade by the inclusion of deaths which are not affected by the basic characteristics of the tumour.

**Table 5-9:** Unadjusted hazard ratios for histological grade, considering breast cancer deaths only, 1982-1998.

Grade	Haz. Ratio	95% Conf. Interval
1	1.00	-
2	3.43	2.32-5.06
3	7.39	5.06-10.80

**Table 5-10:** The effect of social class (unadjusted) on breast cancer survival, considering breast cancer deaths only. 1982-1998.

Social class	Haz. Ratio	95% Conf. Interval
High	1.00	-
Low	1.40	1.23-1.59

Table 5-10 shows the unadjusted effect of social class on survival to death from breast cancer. The estimated hazard ratio for the lower social classes was 1.40, highly significant, and showing an effect of greater size than observed using all causes of death as the endpoint. It is also larger than the hazard ratio observed in the smaller tumour series from 1982-93.

**Table 5-11:** The effect of Deprivation (unadjusted) on breast cancer survival, considering breast cancer deaths only. 1982-1998.

<b>Deprivation</b>	<b>Haz. Ratio</b>	<b>95% Conf. Interval</b>
<b>Most affluent</b>	1.00	-
<b>2</b>	1.04	0.92-1.18
<b>3</b>	1.03	0.91-1.17
<b>4</b>	1.04	0.91-1.20
<b>Most deprived</b>	1.21	1.00-1.48

Table 5-11 shows the unadjusted effect of deprivation category on survival to death from breast cancer. The effect of deprivation was similar to that observed in the initial analysis in table 4-1. The most deprived women had a borderline significant hazard ratio of 1.21.

Table 5-12 reports the estimated hazard ratio and 95% confidence interval associated for deprivation categories after adjusting for grade, for breast cancer deaths only. Although the hazard ratio estimate for the most deprived category was no longer significant when adjusted for grade, it is of the same magnitude as the unadjusted estimate. Also, the hazard ratio for the second most deprived category has increased with adjustment for grade. We cannot therefore conclude that the effect of deprivation on survival can be accounted for by a difference among deprivation categories with respect to histological grade.

**Table 5-12:** The effect of deprivation (based on residential area) on breast cancer survival, adjusted for grade, considering breast cancer deaths only. 1982-1998

Factor/category		Haz. Ratio	95% Conf. Interval
Grade	1	1.00	-
	2	3.40	2.30-5.02
	3	7.33	5.02-10.71
Deprivation	Most affluent	1.00	-
	2	1.06	0.84-1.34
	3	1.09	0.86-1.38
	4	1.26	0.98-1.61
	Most deprived	1.23	0.87-1.75

**Table 5-13:** The effect of Social class on breast cancer survival, adjusted for grade, considering breast cancer deaths only. 1982-1998.

Factor/category		Haz. Ratio	95% Conf. Interval
Social class	High	1.00	-
	Low	1.48	1.19-1.84
Grade	1	1.00	-
	2	4.13	2.27-7.49
	3	9.61	5.38-17.18



Table 5-13 reports the estimated hazard ratios associated with lower social class after adjusting for grade, taking only breast cancer deaths as failure events. The hazard ratio for lower social classes increased from 1.40 (CI, 1.23-1.59) to 1.48 (CI, 1.19-1.84) when adjusted for grade. This finding might again suggest that grade is a negative confounder of social class, or it may be a chance finding. At any rate, the poorer survival of women in the lower social classes cannot be attributed to differences in histological grade on the basis of these results.

## 5.4. Discussion

Table 5.14 summarises the findings of sections 5.2 and 5.3. It can be seen that the role of tumour grade in explaining the effect of deprivation and social class on breast cancer survival was not considerably substantial for either failure endpoint in our study. After using all the available data to increase the sample size, we found that grade does not account for the effect of social class or for that of deprivation category. Indeed, the hazard ratios associated with lower social class or deprivation actually increased somewhat after adjustment for grade. This result might suggest histological grade as a negative confounder of social class and deprivation. As regards social class, Table 5-2 shows some weak evidence for this, in that there were slightly fewer grade 3 tumours in the lower social classes, but this difference was not substantial or statistically significant. There may therefore be weak negative confounding of grade with social class, but this cannot be reliably distinguished from random variation. Table 5-3 suggests if anything *positive* confounding of deprivation category with grade, in that there are slightly fewer grade 1 tumour in the two most deprived categories.

**Table 5-14:** Grade-adjusted and unadjusted effects of socioeconomic status, stratified by death endpoint (breast cancer or all causes) measure of socioeconomic status (social class and deprivation categories).

Socioeconomic status category	Adjusted?	All deaths		Breast cancer deaths	
		H.R	95% CI	H.R	95% CI
Lower social class	Yes	1.33	1.15-1.56	1.48	1.19-1.84
	No	1.25	1.16-1.36	1.40	1.23-1.59
Most deprived	Yes	1.49	0.90-1.46	1.23	0.87-1.75
	No	1.26	1.15-1.40	1.21	1.00-1.48

Our results suggest, therefore that differences in histological grade of the tumours does not account for socioeconomic differences in survival. However, our interpretation must be qualified by the fact that these results came from analyses of that minority of cases with data on grade, including tumours diagnosed more recently. That minority may not be representative, and follow-up for the most recent cases may not be complete. Future analyses of data when reliable long-term follow-up is available on cases diagnosed since the 1990's, when grade is routinely recorded on the majority of tumours, will yield more conclusive results.

# CHAPTER 6

## Discussion, conclusions and implications for future work

The major finding of this work is that we could not wholly or even largely account for socioeconomic effects on breast cancer survival by pathological factors including disease stage, morphology or grade. We used two socioeconomic measures in this study, one an area-of-residence-based deprivation index, the other the traditional occupation-based social class. The area-based deprivation score used was the Carstairs' Index. This is a proxy measure of deprivation, based on small area measures of overcrowding, unemployment, social class (occupation) and car ownership. It has been shown that area-based deprivation has a stronger association with cancer mortality than the occupation-based social class (Carstairs et al 1991). In addition, the Carstairs index was shown to adjust more fully for socioeconomic imbalances in the Edinburgh Breast Screening Trial (Alexander et al, 1998; Alexander et al, 1999).

Several studies have examined the effect of area-based deprivation on disparity of survival in breast cancer patients (Schrijvers et al 1995 a; Carnon et al 1994; Garvican et al 1998).

Despite this, the effect of socioeconomic status on breast cancer survival remains a complex issue. Patients of low socioeconomic status tend to have poorer survival from many other diseases, so it is very likely that there is a complex mix of host, environmental and healthcare delivery factors involved in the poorer prognosis. Researchers noted as early as 1977 the importance of host factors in the poorer survival of patients of low socioeconomic status (Berg et al, 1977).

The results of this study add further to the evidence of an increased risk of death in breast cancer patients of low socioeconomic status, whether measured occupationally as social class or by an area-based method. They also suggest that this increased risk is not entirely attributable to morphological type or stage of disease. Although stage tends to account for more of the effect, particularly of the social class measure, there is still a substantial proportion of the effect unaccounted for by stage or by stage and morphology both together. This is consistent with the findings of Thomson et al (2001), who observed that oestrogen receptor status and treatment factors accounted for only 20% of the difference in survival between patients of high and low socioeconomic status (as measured by area of residence). Similarly, Newman et al (2002) found that the survival differences by ethnic group in the US could not be accounted for by stage of disease. Similarly, Ansell et al (1993) found that despite significantly poorer stage in black American women, this still did not explain the poorer survival of the latter group. Interestingly, Bassett and Krieger (1986), also studying US black and white women, found that socioeconomic status was a more important prognostic factor in breast cancer than ethnic group and indeed that socioeconomic status explained most of the survival difference between black and white women. This was also suggested by the study of Gordon et al (1992) and the earlier work of Berg et al (1977). In Finland, Karjalainen et al (1990) found social class to be a significant prognostic factor in breast cancer survival, and its effect was only partly explained by differences in stage of tumour at the time of diagnosis.

One point which should be made is that stage of disease is a classification of a continuous tumour burden into a number of discrete classes, some of which are very broad. There is, for example, considerable scope for residual effects and residual confounding with socioeconomic status within stage II disease, which can encompass tumours of sizes 2 to 5 cm. Thus a more

detailed measure of the state of advancement of the tumour, involving size and lymph node status, including number of involved lymph nodes, might account for considerably more of the socioeconomic effects on survival.

Nevertheless, we did find significantly poorer stage at presentation in patients of lower socioeconomic status, and this accounted for some of the differences in survival. This is in disagreement with the findings of Carnon et al (1994), who reported no significant differences between socioeconomic groups with respect to tumour size or node status. Ansell et al (1993) also reported no significant differences between blacks and whites with regard to stage at the time of diagnosis. Our results are, however, partly consistent with those of Macleod et al (2000a) who reported a higher rate of clinically determined locally advanced disease in patients resident in deprived areas. Mandelblatt et al (1991) also found that breast cancer patients of low socioeconomic status were at high risk of late stage disease. Brewster et al (2001) reported no significant differences in stage among socioeconomic groups, but a reanalysis of their tabular data on tumour size in breast cancer patients shows a significant trend of increasing size with deprivation ( $\chi^2=5.17$ , 1 degree of freedom,  $P=0.02$ ). Thus, there is some support in the literature for our observed association of stage and socioeconomic status.

The poorer stage in women of lower socioeconomic status may be addressed by screening, but it is unlikely in this data set to be explained by differential uptake of screening. This is because most of our tumours were diagnosed before screening was widespread in East Anglia.

In this study, the distribution of morphological type was associated with socioeconomic status, but it is difficult to interpret this since 40% of the cases were classified simply as

adenocarcinoma or 'other'. An association of morphological type with socioeconomic status is not entirely unexpected, since Thomson et al (2001) found a significant association between deprivation category and oestrogen receptor status. More thorough morphological typing might account for more of the survival effect of socioeconomic status.

Only limited information was available from East Anglian Cancer Registry records for histological grade, although in recent years, histological grade has been registered in the majority of cases. Therefore the findings of this study with respect to grade must be interpreted with caution because of the large percentage with grade missing, and the short follow-up on average of those with grade known. At any rate, tumour grade in this study does not account for the effect of either social class or deprivation on survival. There remain some uncertainties, as only 2666 subjects in total have both grade and social class recorded. When further follow-up of recent cases becomes available, it will be possible to assess with more confidence the extent to which histological grade may account for socioeconomic differences in survival. Since it is known that some risk factors, notably family history, vary in their effect on risk by histological grade (Duffy et al, 1999) and it is likely that in some cases, histological grade may actually deteriorate as the tumour grows (Tabar et al, 1996), there is at least a possibility that grade is implicated in the prognostic effect of socioeconomic status.

The association of social class with survival was essentially manifested as a threshold effect, a difference between the non-manual and manual occupations. The association of deprivation category was essentially an increased hazard of death for the most deprived category, and very little difference in risk among the other four categories.

The association of survival with socioeconomic status (measured by either means) remained significant or close to significant after adjustment for stage or morphological type or both. It is notable that the adjustment accounted for a greater proportion of the survival effect for death from any cause than for breast cancer as the underlying cause of death. This may be due to misclassification of cause of death, a direct effect of tumour attributes on deaths from other causes or an increased risk of death from other causes in association with more aggressive treatment of more advanced tumours. Also, it is of interest that whereas deprivation category was not significant as a predictor of breast cancer death (although it was so for all-cause deaths), its effect was more robust to adjustment. Stage accounted for at least part of the effect of social class but for none of the effect of deprivation category, suggesting that the non-occupational aspects of poverty captured by the deprivation score are associated with survival independently of stage of disease. This may be related to either host factors that affect survival generally or poorer access to prompt and appropriate therapy.

In the survival analysis for the deprivation category, the most striking result was that rather than a smooth trend with deprivation, the lowest category had poorer survival, and the other four categories had similar survival to each other. It is not clear why this should be. Further studies with individual rather than area-based deprivation measures might clarify this.

Among the most deprived and lowest social class patients, in addition to stage at diagnosis, impairment of host resistance could be related to lower social support, nutritional disadvantage, and psychological factors. There are also some aspects of the health care system which could be related to the lower survival of the lower socioeconomic groups. These include; type of treatment, its quality and appropriateness, adverse hospital referral patterns of treatment and worse compliance with treatment in this group of patients. Poorer compliance

with treatment is unlikely to be an explanation, however, since the vast majority of breast cancer patients complete their recommended course or courses of therapy. For most of these factors, appropriate information is not available from routine registry data. Therefore prospective analytic studies will need to be designed to investigate their impact on survival and the extent to which they account for socioeconomic effects on survival.

The conclusions of the above are:

1. Survival rates in East Anglia confirm the poorer survival of breast cancer patients of lower socioeconomic status.
2. Although, this is not fully accounted for by differences in stage at presentation and morphological type, stage does account for at least a proportion of the poorer survival of women of low socioeconomic status , and the latter may be amenable to improve access to and uptake of screening.
3. Assessment of the extent to which histological grade and other biological features account for the poorer survival of patients with lower socioeconomic status is a target for future research.
4. More detailed classification of stage of disease, including separate classification of tumour size and node status, may account for a greater proportion of the socioeconomic effects.
5. Research is needed on access to, and timing of and compliance with appropriate treatment in relation to socioeconomic status. This will require ad hoc prospective studies, as will 6 and 7 below.
6. Taken together, the findings of this study suggest that the socioeconomic status can account for at least part of observed differences in breast cancer survival. It would be useful to confirm these findings in additional studies that include other individual



socioeconomic indices in addition to area-based and occupational measures. These might include educational status.

7. It has been observed that patients of lower socioeconomic status have poorer survival in many chronic diseases in addition to breast cancer. There is therefore scope for research on measures of general health status and their joint association with both socioeconomic status and survival from breast cancer and other diseases.

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